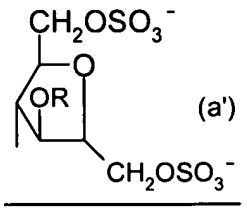
IN THE CLAIMS

This listing of claims replaces all prior versions, and listings, in this application.

1. (withdrawn-currently amended) A process for the preparation of a depolymerized-LMW-epiK5-N,O-sulfate containing 40%-60% iduronic units and having a sulfation degree of from 2.3 to 2.9 and characterized by the structure (a')



(a')

in which R represents hydrogen or SO_3^- at the reducing end of the majority of its chains, which comprises

(a) treating a tertiary or quaternary organic base salt of a depolymerized-LMW-epiK5-N-sulfate containing 40%-60% iduronic units with a sulfation agent under O-oversulfation conditions to obtain a depolymerized-LMW-epiK5-amine-O-oversulfate, [[;]]

(b) submitting the depolymerized-LMW-epiK5-amine-O-oversulfate thus obtained to a selective O-desulfation to obtain a depolymerized-LMW-epiK5-amine-O-sulfate, [[;]]

(c) treating a tertiary or quaternary organic base salt of the depolymerized-LMW-epiK5-amine-O-sulfate thus obtained with a O-sulfation agent to obtain a depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate, [[;]] and

(d) submitting the depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate thus obtained to a N-sulfation reaction and isolating the depolymerized-LMW-epiK5-N,O-sulfate thus obtained;

wherein (a) comprises

(a1) treating a depolymerized-LMW-epiK5-N-sulfate, in acidic form, with a tertiary or quaternary organic base for 30-60 minutes, maintaining the pH at about 7 by addition of the tertiary or quaternary organic base, and isolating an organic base salt of the depolymerized-LMW-epiK5-N-sulfate and

(a2) treating the organic base salt of the depolymerized-LMW-epiK5-N-sulfate with an O-sulfation agent under O-oversulfation conditions and isolating the depolymerized-LMW-epiK5-amine-O-oversulfate.

2. (withdrawn) The process according to claim 1, wherein the depolymerized-LMW-epiK5-N,O-sulfate thus obtained is isolated as the sodium salt thereof which is optionally converted into another pharmaceutically acceptable salt thereof.

3. (withdrawn) The process according to claim 2, wherein said other salt is that with another alkaline metal, an alkaline-earth metal, aluminum or zinc.

4. (withdrawn) The process according to claim 1, wherein the starting depolymerized-LMW-epiK5-N-sulfate is obtained by submitting a K5-N-sulfate, in any order,

(i) to C5-epimerization with a D-glucuronyl C5-epimerase isolated, purified and either in solution or immobilized on a solid support, at a pH of approximately 7, at a temperature of approximately 30°C and for a time period of 12-24 hours in the presence of at least one bivalent ion selected among calcium, magnesium, barium and manganese; and

(ii) to a nitrous depolymerization followed by reduction, normally with sodium borohydride.

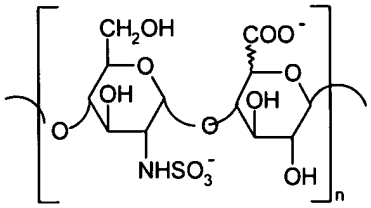
5. (withdrawn) The process according to claim 4, wherein the starting depolymerized-LMW-epiK5-N-sulfate is obtained according to the sequence (i)-(ii) and has a mean molecular weight of from about 1,500 to about 12,000.

6. (withdrawn) The process according to claim 5, wherein, said mean molecular weight is from about 1,500 to about 7,500.

7. (withdrawn) The process according to claim 4, wherein the starting depolymerized-LMW-epiK5-N-sulfate is obtained according to the sequence (ii)-(i) and has a mean molecular weight of from about 4,000 to about 12,000.

8. (withdrawn) The process according to claim 7, wherein said molecular weight is of from about 5,000 to about 7,500.

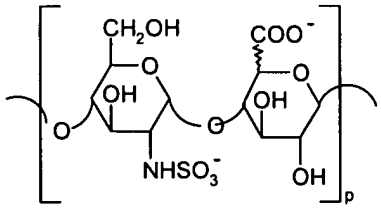
9. (withdrawn) The process according to claim 1, wherein the starting depolymerized-LMW-epiK5-N-sulfate consists of a mixture of chains in which at least 90% of said chains has the formula I



(I)

in which 40%- 60% of the uronic units are those of iduronic acid, n is a integer from 2 to 20 and the corresponding cation is chemically or pharmaceutically acceptable.

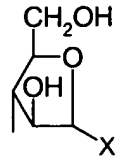
10. (withdrawn) The process according to claim 1, wherein said starting depolymerized-LMW-epiK5-N-sulfate consists of a mixture of chains in which the preponderant species has the formula I'a



(I'a)

wherein 40% to 60% of the uronic units are those of iduronic acid and p is an integer from 4 to 8.

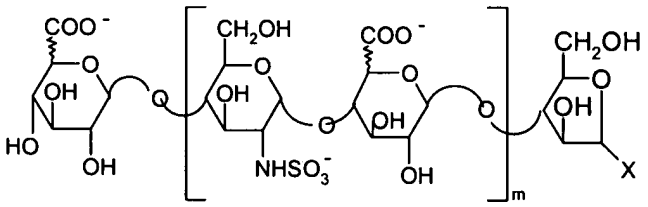
11. (withdrawn) The process according to claim 1, wherein said starting depolymerized-LMW-epiK5-N-sulfate presents a 2,5-anhydromannitol unit of structure (a)



(a)

in which X represents a hydroxymethyl group, at the reducing end of the majority of the chains in said mixture of chains.

12. (withdrawn) The process according to claim 9, wherein said starting depolymerized-LMW-epiK5-N-sulfate consists of a mixture of chains in which the preponderant species has the formula I'b



(I'b)

in which X hydroxymethyl, m is 4, 5 or 6, the corresponding cation is a chemically or pharmaceutically acceptable ion and the glucuronic and iduronic units are present alternately, the non reducing extremity being a glucuronic or iduronic unit, with a ratio glucuronic/iduronic from 45/55 to 55/45.

13. (withdrawn) A process for the preparation of depolymerized-LMW-K5-N,O-sulfates having a sulfation degree of from 2.3 to 2.9 and of their pharmaceutically acceptable salts, which comprises

(ii) submitting a K5-N-sulfate to a nitrous depolymerization to obtain a depolymerized-LMW-K5-N-sulfate having a mean molecular weight higher than 4,000;

(i) submitting the depolymerized-LMW-K5-N-sulfate thus obtained to a C5-epimerization with D-glucuronyl-C5-epimerase to obtain a depolymerized-epiK5-N-sulfate containing from 40% to 60% iduronic units;

(a) treating a tertiary or quaternary organic base salt of the depolymerized-LMW-epiK5-N-sulfate thus obtained with a sulfation agent under the conditions of O-oversulfation to obtain a depolymerized-LMW-epiK5-amine-O-oversulfate;

(b) submitting the depolymerized-LMW-epiK5-amine-O-oversulfate thus obtained to a selective O-desulfation to obtain a depolymerized-LMW-epiK5-amine-O-sulfate;

(c) treating a tertiary or quaternary organic base salt of the depolymerized-LMW-epiK5-amine-O-sulfate thus obtained with a O-sulfation agent to obtain a depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate; and

(d) submitting the depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate thus obtained to a N-sulfation reaction and isolating the depolymerized-LMW-epiK5-N,O-sulfate thus obtained as the sodium salt thereof which is optionally converted into another pharmaceutically acceptable salt.

14. (withdrawn) The process according to claim 13, wherein at the end of step (ii) a depolymerized-LMW-K5-N- sulfate having a mean molecular weight of from about 5,000 to about 7,500 is obtained.

15. (withdrawn) The process according to claim 13, wherein at the end of step (ii) a depolymerized-LMW-K5-N- sulfate having a mean molecular weight of from about 6,000 to about 7,500 is obtained.

16. (withdrawn) A process for the preparation of depolymerized-LMW-K5-N,O-sulfates having a sulfation degree of from 2.3 to 2.9 and of their pharmaceutically acceptable salts, which comprises

(i) submitting a K5-N-sulfate to a C5-epimerization with a D-glucuronyl C5-epimerase isolated, purified and in solution or immobilized on a solid support, at

a pH of about 7, at a temperature of about 30°C and for a period of time of 12-24 ore in the presence of at least one bivalent ion selected among calcium, magnesium, barium and manganese;

(ii) submitting the epiK5-N-sulfate thus obtained to a nitrous depolymerization followed by a reduction, normally with sodium borohydride, to obtain a depolymerized-LMW-K5-N-sulfate;

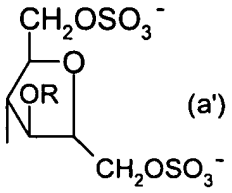
(a) treating a tertiary or quaternary organic base salt of the depolymerized-LMW-epiK5-N-sulfate thus obtained with a sulfation agent under O-oversulfation conditions to obtain a depolymerized-LMW-epiK5-amine-O-oversulfate;

(b) submitting the depolymerized-LMW-epiK5-amine-O-oversulfate thus obtained to a selective O-desulfation to obtain a depolymerized-LMW-epiK5-amine-O-sulfate;

(c) treating a tertiary or quaternary organic base salt of the depolymerized-LMW-epiK5-amine-O-sulfate thus obtained with an O-sulfation agent to obtain a depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate; and

(d) submitting the depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate thus obtained to a N-sulfation reaction and isolating the depolymerized-LMW-epiK5-N,O-sulfate thus obtained as the sodium salt thereof which is optionally converted into another pharmaceutically acceptable salt.

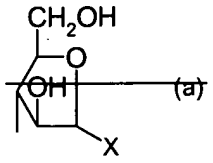
17. (currently amended) A depolymerized-LMW-epiK5-N,O-sulfate containing 40%-60% iduronic units, having a sulfation degree of from 2.3 to 2.9 and characterized by the structure (a')



(a')

in which R represents hydrogen or SO_3^- at the reducing end of the majority of its chains, obtainable according to a process which comprises

(a) treating a tertiary or quaternary organic base salt of a [[the]] depolymerized-LMW-epiK5-N-sulfate containing 40%-60% iduronic units ~~and characterized by the structure (a)~~



~~in which X represents a hydroxymethyl group, at the reducing end of the majority its chains,~~ with a sulfation agent under O-oversulfation conditions to obtain a depolymerized-LMW-epiK5-amine-O-oversulfate, [[;]]

(b) submitting the depolymerized-LMW-epiK5-amine-O-oversulfate thus obtained to a selective O-desulfation to obtain a depolymerized-LMW-epiK5-amine-O-sulfate, [[;]]

(c) treating a tertiary or quaternary organic base salt of the depolymerized-LMW-epiK5-amine-O-sulfate thus obtained with a O-sulfation agent to obtain a depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate, [[;]] and

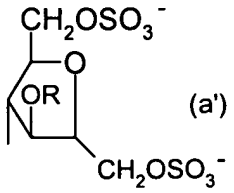
(d) submitting the depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate thus obtained to a N-sulfation reaction and isolating the depolymerized-LMW-epiK5-N,O-sulfate thus obtained;

wherein (a) comprises

(a1) treating a depolymerized-LMW-epiK5-N-sulfate, in acidic form, with a tertiary or quaternary organic base for 30-60 minutes, maintaining the pH at about 7 by addition of the tertiary or quaternary organic base, and isolating an organic base salt of the depolymerized-LMW-epiK5-N-sulfate and

(a2) treating the organic base salt of the depolymerized-LMW-epiK5-N-sulfate with an O-sulfation agent under O-oversulfation conditions and isolating the depolymerized-LMW-epiK5-amine-O-oversulfate.

18. (original) A depolymerized-LMW-epiK5-N,O-sulfate having a sulfation degree of from 2.3 to 2.9, a mean molecular weight of from about 1,500 to about 12,000 and, at the reducing end of the majority of its chains, the structure (a')



(a')

in which R represents hydrogen or SO_3^-, or a pharmaceutically acceptable salt thereof.

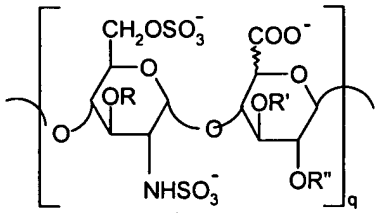
19. (previously presented) The depolymerized-LMW-epiK5-N,O-sulfate according to claim 18, having a mean molecular weight of from about 1,500 to about 8,000 and a sulfation degree from 2.5 to 2.9.

20. (previously presented) The depolymerized-LMW-epiK5-N,O-sulfate according to claim 19, having a sulfation degree of from 2.7 to 2.9.

21. (previously presented) The depolymerized-LMW-epiK5-N,O-sulfate according to claim 20, having a mean molecular weight of about 6,000.

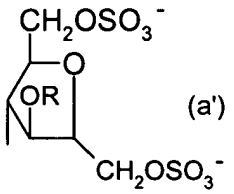
22. (previously presented) The depolymerized-LMW-epiK5-N,O-sulfate according to claim 18, having a mean molecular weight of about 6,000, a sulfation degree of from 2.7 to 2.9, a content of 80%-95% in glucosamine 6-O-sulfate, of 95%-100% in glucosamine N-sulfate, of 45%-55% in glucosamine 3-O-sulfate, of 35%-45% in glucuronic acid 3-O-sulfate, of 15%-25% in iduronic acid 2-O-sulfate, or a pharmaceutically acceptable salt thereof.

23. (previously presented) The depolymerized-LMW-epiK5-N,O-sulfate according to claim 18 consisting of a mixture of chains in which at least 80% of said chains has the formula III



(III)

wherein the 40%-60% of the uronic units are those of iduronic acid, q is an integer from 2 to 17, R, R' and R" are hydrogen or SO_3^- for a sulfation degree of from 2.3 to 2.9, and the reducing end of the majority of the chains in said mixture of chains presents a sulfated 2,5-anidromannitol unit of structure (a')



(a')

in which R represents hydrogen or SO_3^- and the corresponding cation is chemically or pharmaceutically acceptable.

24. (previously presented) The depolymerized-LMW-epiK5-N,O-sulfate according to claim 23, consisting of a mixture of chains in which at least 80% of said chains has the formula III wherein q is an integer from 2 to 14.

25. (previously presented) The depolymerized-LMW-epiK5-N,O-sulfate according to claim 23, consisting of a mixture of chains in which at least 80% of said chains has the formula III wherein q is an integer from 2 to 11.

26. (previously presented) The depolymerized-LMW-epiK5-N,O-sulfate according to claim 23, consisting of a mixture of chains in which the preponderant species is a compound of formula III wherein q is 8 or 9, R is 45%-55% SO_3^-, R' is 35%-45% SO_3^- in glucuronic acid, R" is 15%-25% SO_3^- in iduronic acid, for a sulfation degree of from 2.7 to 2.9.

27. (previously presented) A pharmaceutical composition comprising, as an active ingredient, a pharmacologically active amount of a depolymerized-LMW-epiK5-N,O-sulfate according to claim 17, or of a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutical carrier.

Claims 28-35 (canceled)